REMARKS

The present Amendment and the following Remarks are submitted in response to the Office Communication mailed May 3, 2006. Applicant thanks the Examiner for entering the previous amendment to the claims, for reviewing the information disclosure statement and for approving the drawings. Applicant also thanks the Examiner for agreeing to the relationships among the groups of claims and for adjusting the Restriction Requirement accordingly.

In regard to claim 59, Applicant is adjusting the approach and requesting reconsideration of the decision not to examine this claim. The Examiner claims a serious burden for searching for art on the dominant negative mutant. In response, Applicant is amending claim 59 to limit the mutant's variation from the sequence searched as SEQ ID NO:4 and fragments thereof but which have an alternate residue at position 111. Applicant believes that a dominant negative mutant of claim 59 would be detected on the searches identifying art for SEQ ID NO:4 and claim 30, when one focuses on residue 111. As the same search would be used, Applicant respectfully requests that the Examiner agree that the amendment to claim 59 relieves the burden and proceed with examining this amended claim.

Claims 30, 34 and 59 are being amended. Support for the amendment to claim 30 can be found in the specification, for example, at the paragraph on page 30, line 22 to page 31, line 21. Support for the amendment to claim 34 can be found in the specification, for example, at page 10, lines 16-18. Support for the amendment to claim 59 can be found in the specification, for example, at the paragraph on page 32, line 21 to page 33, line 14. Claims 34, 36, 38, and 59-64 are withdrawn. Claim 37 is being canceled. Claims 30, 31, 34, 36, 38, 56 and 59-64 are pending upon entry of these amendments.

No new matter is being added. The Objection and Rejections raised by the Examiner in the Communication are addressed below.

Paragraph 4. Title

The Examiner objected to the title as apparently not being descriptive. Applicant herein amends the title to reflect the claimed subject matter.

Paragraph 5. Related Applications Update

The Examiner objected to the apparent failure to update the biographical information in the specification. Applicant respectfully directs the Examiner's attention to the amendments to the specification submitted with the Response to the Restriction Requirement on April 11, 2006. Those amendments included the update requested in this objection. Applicant requests entry of the amendments to the specification submitted on April 11, 2006 and withdrawal of this objection.

Paragraph 6. Claim Objection

The Examiner objected to claims 30, 31 and 56 for containing abbreviations of recited terms. Applicant herein amends claim 30 to spell out the words to define the abbreviations so the abbreviations can be retained in the subsequent claims. In view of this amendment, withdrawal of this objection is requested.

Paragraph 7. Rejection of the Claims Under 35 U.S.C. §112, First Paragraph

Claims 30 and 56 were rejected under 35 U.S.C. §112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims. Specifically, while the Examiner felt that an NCE1 enzyme of SEQ ID NO:4 is enabled, not all of the embodiments in the rejected claims are enabled. In particular, the Examiner felt that there would be undue experimentation for one of skill in the art to make or use an NCE1 protein at least 95% identical to SEQ ID NO:4 or encoded by a nucleic acid at least 95% identical to SEQ ID NO:3. Applicant respectfully traverses the rejection.

Applicant herein amends claim 30 (claim 56 dependent thereon) to recite that the protein forms a thioester linkage with NEDD8. One of skill in the art would know how to make a polypeptide or nucleic acid sequence with differences from the recited sequence (SEQ ID NO:3 or SEQ ID NO:4) and determine the percent identity with the recited sequence. This knowledge is supplemented by the disclosure at page 30, line 22 to page 31, line 21; page 32, lines 1-20 and page 16, lines 5-8. A common structural feature of an NCE1 protein, the Cysteine at residue 111 of SEQ ID NO:4, further illustrated in Figure 2, is described as important for biological activity as further guidance on how to make non-identical sequences which result in polypeptides with characteristic NCE1 structure and function. International publication WO95/18974 is referenced to establish the state of the art at making functional variants of a protein. That publication, B1 of the supplemental IDS, at pages 32, line 35 to page 38, line 5, describes conservative amino acid substitutions not likely to have a major effect on the biological activity. The publication also describes the use of aligned homologs of the subject protein to generate degenerate sequences of a nucleic acid and thus protein. In the present application, Figures 3 and 7 provide alignments of NCE1 homologs and identify conserved residues for this endeavor. How to determine whether the resulting protein variant performs the recited thioester linkage function is described in the specification at Example 8, page 45. Applicant believes that the application provides the sequence and assay information to one of skill in the art, being educated by publications such as WO95/18974, to generate and identify the NCE1 variants recited in the claims without undue experimentation. In view of these amendments and remarks, Applicant respectfully requests that this rejection be withdrawn.

Rejection of the Claims Under 35 U.S.C. §102

Claims 30, 31 and 56 were rejected under 35 U.S.C. §102(a), as allegedly being anticipated by Osaka et al.. The Examiner noted a disclosure of SEQ ID NO:4 in provisional application No. 60/096,525 and compared its filing date of August 12, 1998 to the August 1, 1998 apparent publication date of a sequence 100% identical to SEQ ID NO:4 in Osaka et al.. Thus, the Examiner alleged that Osaka et al. anticipates the claimed invention. Applicant respectfully traverses this rejection.

Filed herewith is a Declaration under 37 C.F.R. §1.131 together with Exhibits A-B. The Declaration and Exhibits present evidence that Applicant was in possession of the NCE1 sequence and identified it as a human homolog of yeast Ubc12, and thus a conjugating enzyme with thioester linkage activity before the publication date of Osaka et al.. Therefore, Osaka et al. is not available as prior art under 35 U.S.C. §102(a). In view of these remarks, Applicant respectfully requests that this rejection be withdrawn.

Rejoinder

Applicant submits that claims 30, 31 and 56 will be found allowable, and the application is allowable with respect to the group elected after the Restriction Requirement mailed January 11, 2006. Applicant believes that now, the Examiner, under MPEP § 821.04, as noted in the Restriction Requirement, can undertake the review of the withdrawn process claims, 34, 36, 38 and 60-64, which depend from or otherwise include all the limitations of the allowable product claims. In the next Office communication, Applicant respectfully requests comment on these withdrawn claims after rejoinder.

CONCLUSION

The foregoing amendments and remarks are being made to place the Application, having both elected and rejoined claims, in condition for allowance. Applicant respectfully requests the timely allowance of the pending claims because, in view of these amendments and remarks, Applicant respectfully submits that the objections to the specification and the claims and rejections of the claims under 35 U.S.C. §§ 112 and 102 are overcome. Applicant believes that this application is now in condition for allowance. Early notice to this effect is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned. If the Examiner disapproves of Applicant's amendments and remarks in this response, Applicant requests a prompt mailing of a notice to that effect.

This paper is being filed timely as a request for a three month extension of time is filed concurrently herewith. No additional extensions of time are required. In the event any additional

extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

2 November 2006

MILLENNIUM PHARMACEUTICALS, INC.

Bv

Trace M. Sioussat, Ph.D. Registration No. 50,609 40 Landsdowne Street Cambridge, MA 02139 Telephone - 617-374-7679

Facsimile - 617-551-8820